

Enzyme rhythms in model four_cycle - spontaneous oscillations

Model name: four_cycle

o Optimisation problem

- Protein turnover time $1.8e+03$ s = 30 min
- Perturbed parameter(s) : x1
- Perturbation frequency f : 0.0333/s (period 30 s)
- Scored quantity: v3
- Fitness-averaged fitness
- Posttranslational rhythms allowed
- Standard frequency considered f : 0.0333/s (period 30 s)

o Model properties:

- inactive_enzymes: 0
- balanced_reference_state: 1
- consider_external_rhythm: 1
- adaptive_rhythm: 1
- spontaneous_rhythm: 1
- spontaneous_rhythm_at_omega: 0
- has_spontaneous_rhythm_and_inactive_enzymes: 0

o Beneficial autonomous oscillation found

- Maximum principal synergy found (in tested range) at frequency $f = 0.631/s$ (period 1.58 s)
- Maximum fitness found (in tested range) at frequency $f = 1/s$ (period 1 s)

o Fitness changes after external perturbation at frequency $f = 0.0333/s$

- Change by perturbation alone (xx): $-6.59e-07$
- Change by adaption synergies (xu): 0.000471
- Change by periodic enzyme (uu): -0.000666
- Change by enzyme mean shift (u): $5.76e-10$
- Total fitness change : -0.000196
- Fitness gain by adaption : -0.000195
- Maximum adaptive fitness found (in tested range) at frequency $f = 0.000708/s$ (period $1.41e+03$ s)
- Predicted max. fitness change (adaptive, num. opt, full ampl. constraints) at frequency $f = 0.000708$: 0.000458

o autonomous oscillations?

- No beneficial autonomous oscillations (2nd order, amplitude below 1/2 of mean) found at frequency $f = 0.0333/s$ (principal synergy = -0.0499): Predicted fitness change -0.00864

o Numerical calculation (responsive, $f = 0.0333$)

- Fitness change (fitness-averaged): -0.000457
- Fitness change (state-averaged): -0.000456

o Numerical calculation (adaptive, $f = 0.0333$)

- Fitness change (fitness-averaged): -0.000336
- Fitness change (state-averaged): -0.000225

o Numerical calculation (autonomous rhythm, amplitude below 1/2 of mean, $f = 0.0333$)

- Fitness change (fitness-averaged) : $2.38e-06$
- Fitness change (state-averaged): $2.39e-06$

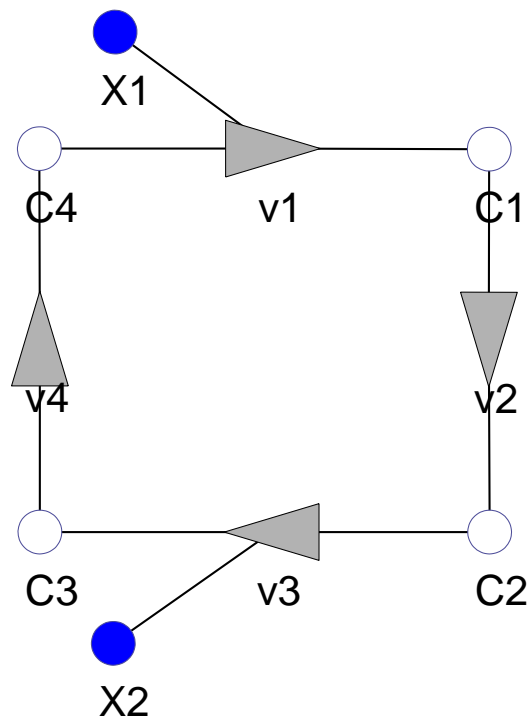
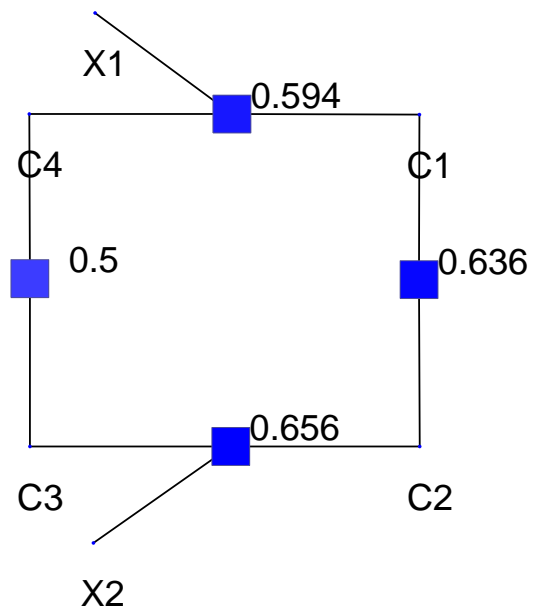
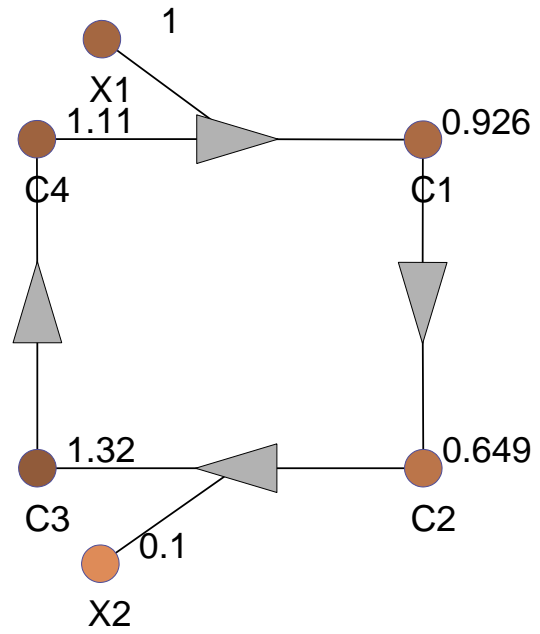


Figure 1: Network and reference flux

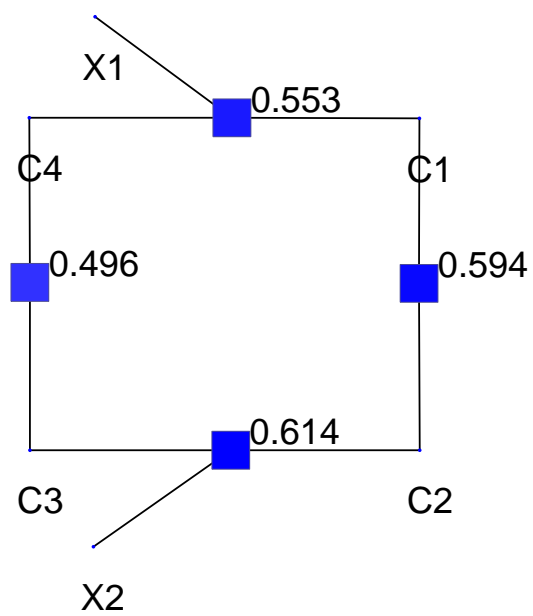
Enzyme levels (reference state)



Metabolite levels (reference state)



Mean enzyme levels



Mean metabolite levels

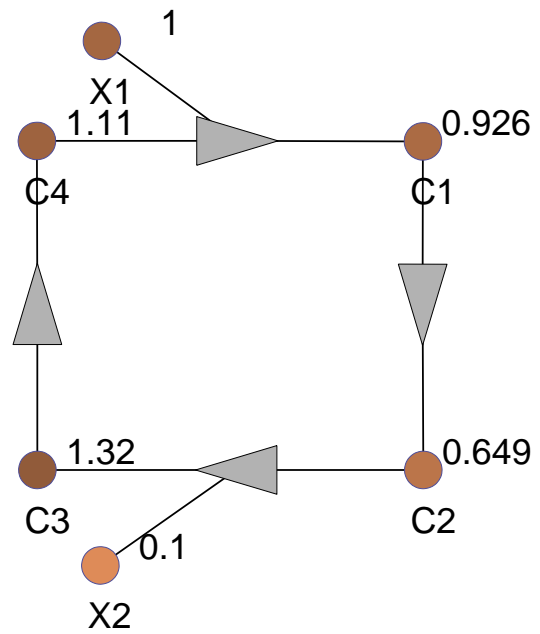


Figure 2: Reference state (top) and mean state during oscillation (bottom).

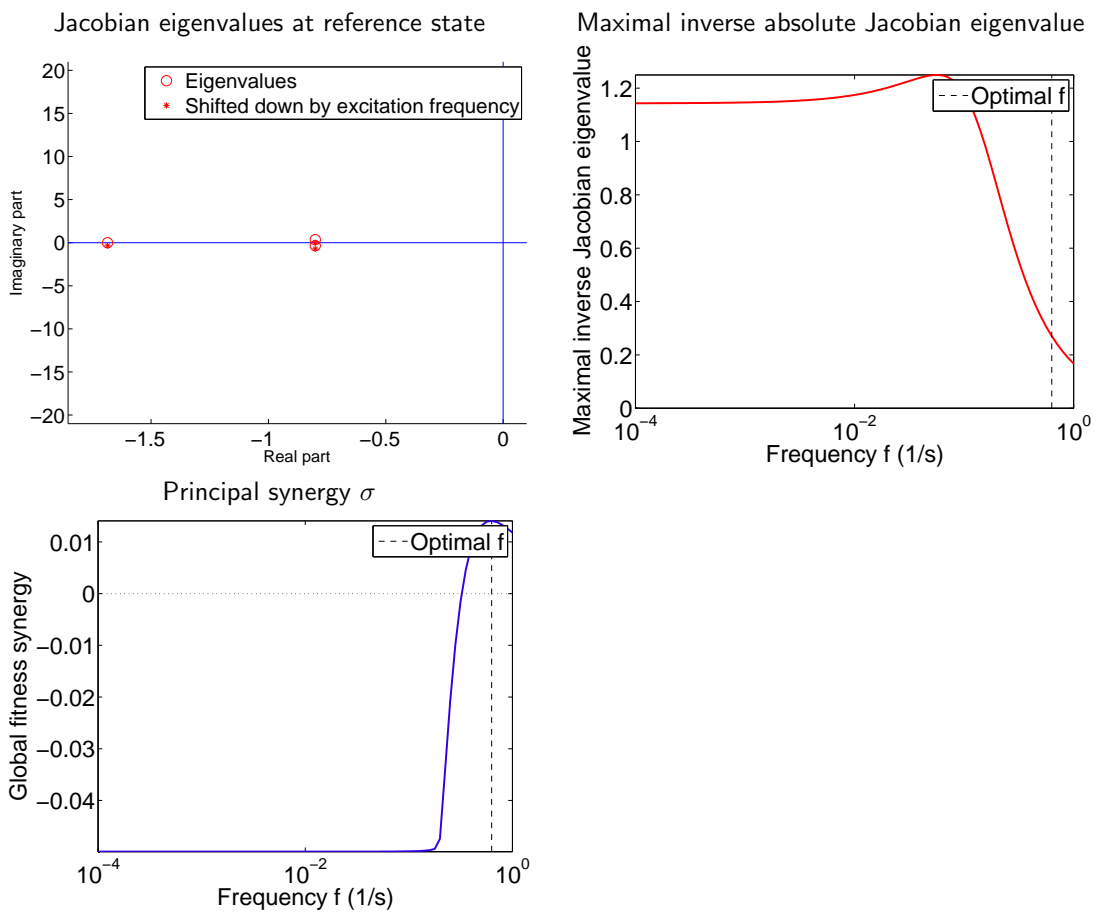
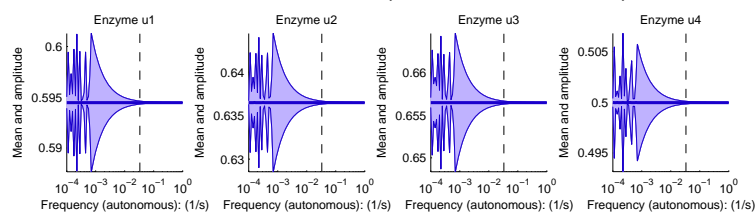
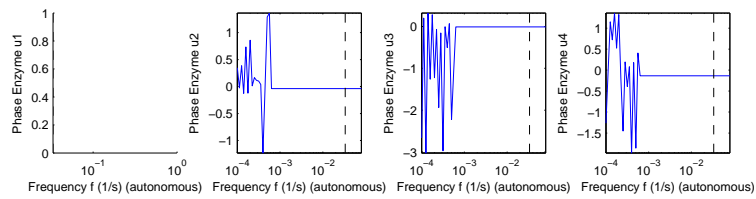


Figure 3: Control analysis: fitness curvatures. Left: Frequency-dependent fitness curvature eigenvalues. Right: relative sizes and phases of the individual enzyme levels (components of the leading fitness curvature eigenvector).

Protein level and enzyme activity (mean and amplitude)



Phase angles $[0, 2\pi]$



Fitness change

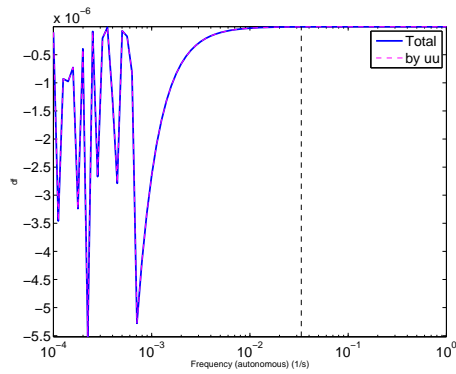


Figure 4: Self-promoting oscillations. Left: amplitudes of protein levels (blue) and modification (grey). Right: phase shifts.

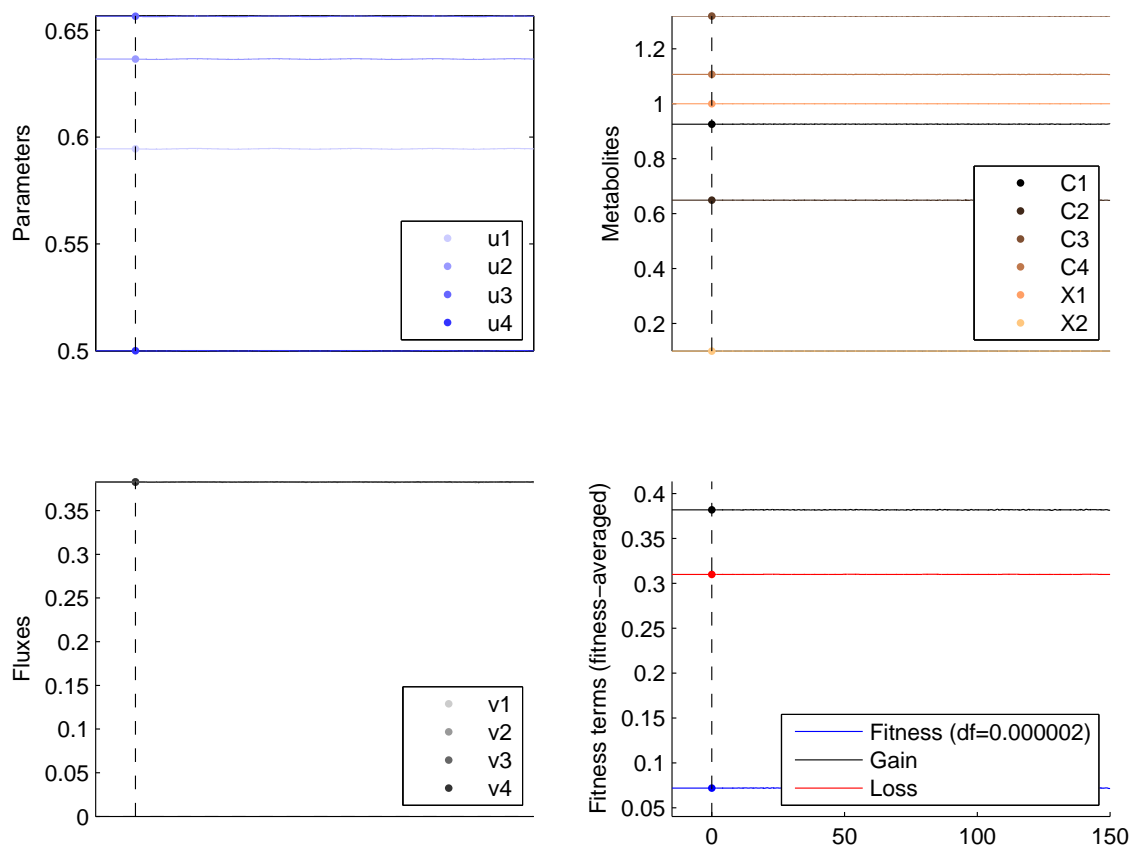
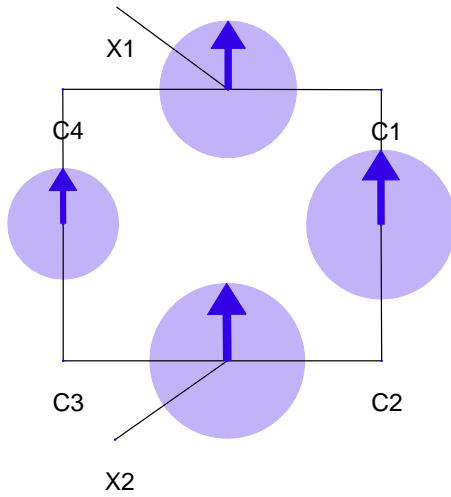
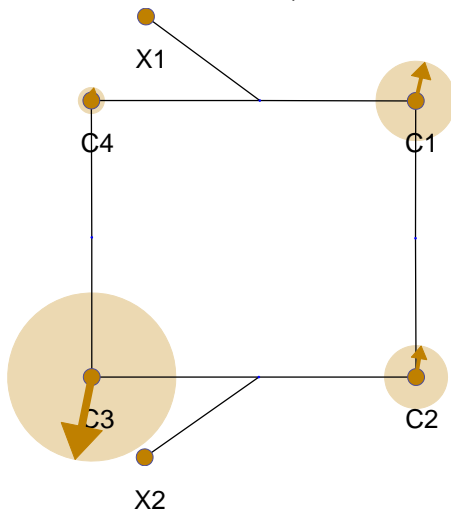


Figure 5: Numerical calculations: spontaneous oscillations. Perturbation frequency see first page.

Enzyme rhythm



Spontaneous oscillations (concentrations)



Spontaneous oscillations (fluxes)

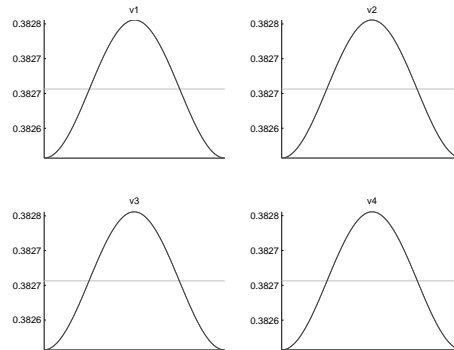
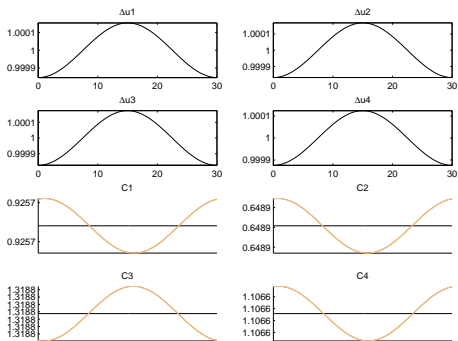
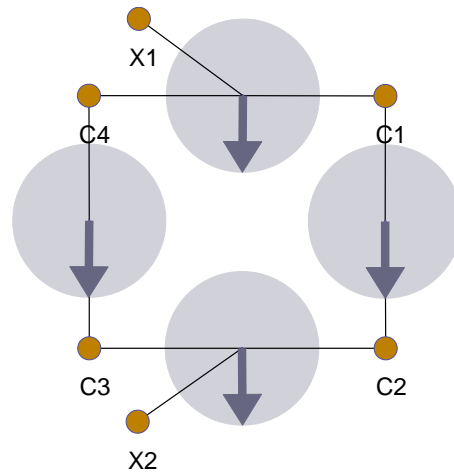


Figure 6: Spontaneous oscillations (local expansion; arrows: absolute changes). Perturbation frequency see first page.

Spontaneous oscillations

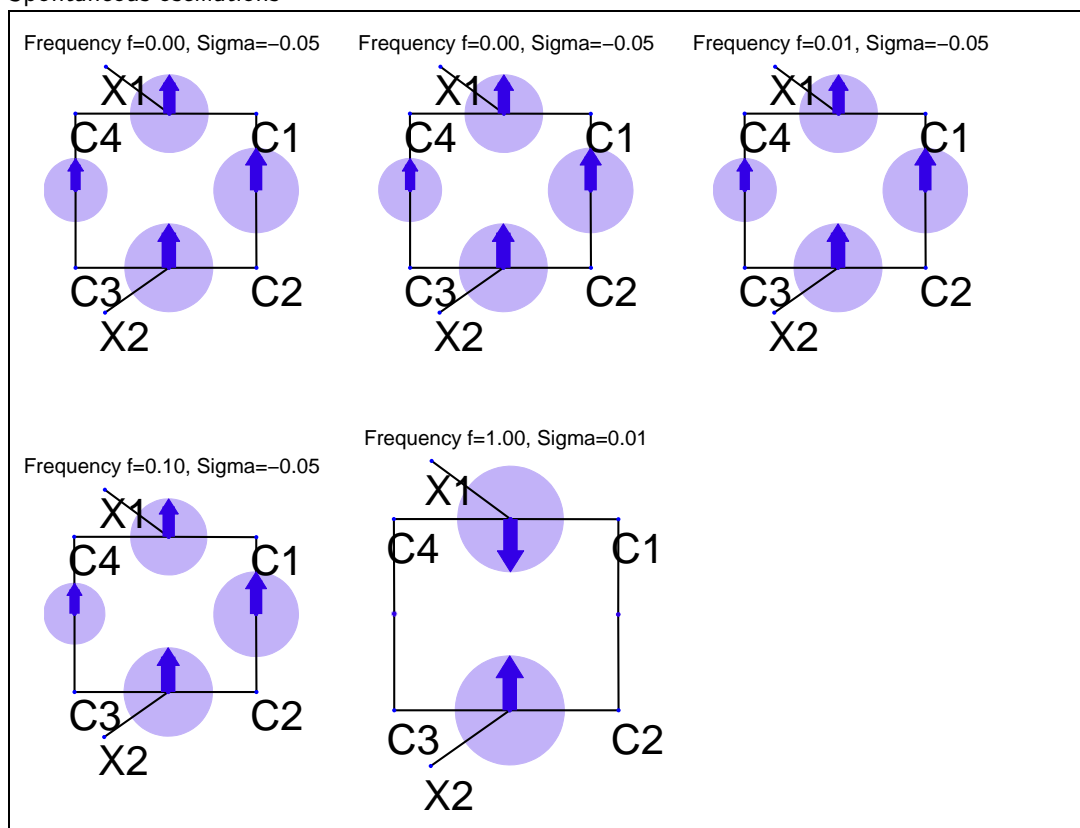


Figure 7: Spontaneous oscillations (or tendencies towards them) for various circular frequencies ω . If the maximal fitness curvatures λ is positive, the rhythm is beneficial (local expansion; arrows: absolute changes).